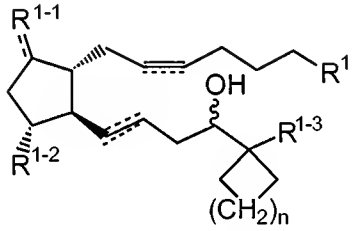
**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

Claims 1-34 (Canceled)

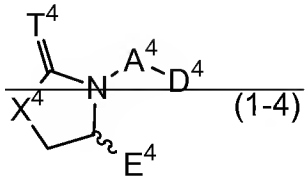
35. (Currently amended) A method for treating cartilage-related disease, which consists of administering a composition consisting of a substance, as an active ingredient, having an EP2 agonist activity selected from a compound represented by formula (1-1)




(1-1)

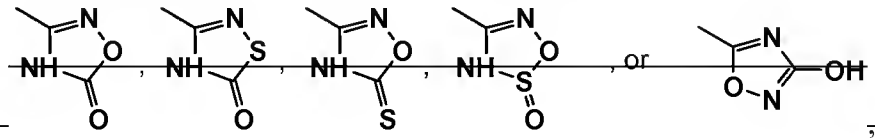
wherein $R^1$ is carboxy or hydroxymethyl, $R^{1-1}$ is oxo, methylene or halogen atom, $R^{1-2}$ is hydrogen atom, hydroxy or C1-4 alkoxy, $R^{1-3}$ is hydrogen atom, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, or C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted by 1-3 substituents selected from the following (1) to (5): (1) halogen atom, (2) C1-4 alkoxy, (3) C3-7 cycloalkyl, (4) phenyl or (5) phenyl substituted by 1-3 substituents selected from halogen atom, C1-4 alkyl, C1-4 alkoxy, nitro or trifluoromethyl; n is 0 or 1-4; with the proviso that (1) when 5-6 position is triple bond, 13-14 position is not triple bond, (2) when 13-14 position is double bond, the double bond represents E form, Z form or mixture of EZ form

or a salt thereof, ~~and a compound represented by formula (1-4)~~



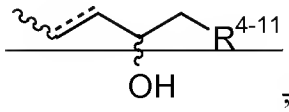
(1-4)

wherein $T^4$ is oxygen atom or sulfur atom, $X^4$ is $-CH_2-$, $-O-$ or $-S-$, $A^4$ is $A^{4-1}$ or $A^{4-2}$, $A^{4-1}$ is C2-8 straight-chain alkylene optionally substituted by 1 to 2 C1-4 alkyl, C2-8 straight-chain alkenylene optionally substituted by 1 to 2 C1-4 alkyl or (3) C2-8 straight-chain alkynylene optionally substituted by 1 to 2 C1-4 alkyl, $A^{4-2}$ is $-G^{4-1}-G^{4-2}-G^{4-3}-$, $G^{4-1}$ is C1-4 straight-chain alkylene optionally substituted by 1 to 2 C1-4 alkyl, C2-4 straight-chain alkenylene optionally substituted by 1 to 2 C1-4 alkyl or C2-4 straight-chain alkynylene optionally substituted by 1 to 2 C1-4 alkyl, $G^{4-2}$ is $-Y^4-$, ring 1, $-Y^4-$ring 1, ring 1-$Y^4-$ or $-Y^4-$C1-4 alkylene ring 1, $Y^4$ is $-S-$, $-SO-$, $-SO_2-$, $-O-$ or $-NR^{4-1}-$, $R^{4-1}$ is hydrogen atom, C1-10 alkyl or C2-10 acyl, $G^{4-3}$ is a bond, C1-4 straight-chain alkylene optionally substituted by 1 to 2 C1-4 alkyl, C2-4 straight-chain alkenylene optionally substituted by 1 to 2 C1-4 alkyl or C2-4 straight-chain alkynylene optionally substituted by 1 to 2 C1-4 alkyl, $D^4$ is $D^{4-1}$ or $D^{4-2}$, $D^{4-1}$ is $-COOH$, $-COOR^{4-2}$, tetrazol-5-yl or $-CONR^{4-3}SO_2R^{4-4}$, $R^{4-2}$ is C1-10 alkyl, phenyl, C1-10 alkyl substituted by phenyl or biphenyl, $R^{4-3}$ is hydrogen atom or C1-10 alkyl, $R^{4-4}$ is C1-10 alkyl or phenyl, $D^{4-2}$ is $-CH_2OH$, $-CH_2OR^{4-5}$, hydroxy, $-OR^{4-5}$, formyl, $-CONR^{4-6}R^{4-7}$, $-CONR^{4-6}SO_2R^{4-8}$, $-CO-$(NH-amino acid residue-CO)$_m$-OH, $-O-$(CO-amino acid residue-NH)$_m$-H, $-COOR^{4-9}$, $-OCO-R^{4-10}$, $-COO-Z^{4-1}-Z^{4-2}-Z^{4-3}$,



, $R^{4-5}$ is C1-10 alkyl, $R^{4-6}$ and $R^{4-7}$ are, each independently, hydrogen atom or C1-10 alkyl, $R^{4-8}$ is C1-10 alkyl substituted by phenyl, $R^{4-9}$ is C1-10 alkyl substituted by biphenyl optionally substituted by 1 to 3

~~substituents selected from C1-10 alkyl, C1-10 alkoxy and halogen atom or biphenyl substituted by 1 to 3 substituents selected from C1-10 alkyl, C1-10 alkoxy and halogen atom, $R^{4-10}$ is phenyl or C1-10 alkyl, m is 1 or 2, $Z^{4-1}$ is C1-15 alkylene, C2-15 alkenylene or C2-15 alkynylene, $Z^{4-2}$ is -CO-, -OCO-, -COO-, -CONR$^{4-Z1}$-, -NR$^{4-Z2}$CO-, -O-, -S-, -SO$_2$-, -SO$_2$-NR$^4$-, -NR$^4$SO$_2$-, -NR$^{4-Z3}$-, -NR$^{4-Z4}$CONR$^{4-Z5}$-, -NR$^{4-Z6}$COO-, -OCONR$^{4-Z7}$- or OCOO-, $Z^{4-3}$ is hydrogen atom, C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, ring $Z^4$ or C1-10 alkoxy, C1~10 alkylthio, C1-10 alkyl-NR$^{4-Z8}$- or C1-10 alkyl substituted by ring $Z^4$, ring $Z^4$ is C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated or 3 to 15 membered mono-, bi- or tri-heterocyclic aryl containing 1 to 4 hetero atoms selected from oxygen, nitrogen and sulfur atom which may be partially or fully saturated, $R^{4-Z1}$, $R^{4-Z2}$, $R^{4-Z3}$, $R^{4-Z4}$, $R^{4-Z5}$, $R^{4-Z6}$, $R^{4-Z7}$ and $R^{4-Z8}$ are, each independently, hydrogen atom or C1-15 alkyl, $R^{4-Z1}$ and $Z^{4-3}$ may be taken together with the nitrogen atom to which they are attached to form 5 to 7 membered saturated mono-heterocyclic ring, and the heterocyclic ring may contain other one hetero atom selected from oxygen, nitrogen and sulfur atom, ring $Z^4$ and the saturated mono-heterocyclic ring formed by $R^{4-Z1}$, $Z^{4-3}$ and the nitrogen atom to which they are attached may be substituted by 1-3 groups selected from C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C1-10 alkyl substituted by C1-10 alkoxy, C1-10 alkylthio and C1-10 alkyl-NR$^{4-Z9}$-; $R^{4-Z9}$ is hydrogen atom or C1-10 alkyl, $E^4$ is $E^{4-1}$ or $E^{4-2}$, $E^{4-1}$ is~~




~~, $R^{4-11}$ is C1-10 alkyl, C1-10 alkylthio, C1-10 alkyl substituted by ring 2 or C1-10 alkyl substituted by -W$^{4-1}$-W$^{4-2}$- ring 2, $W^{4-1}$ is -O-, -S-, -SO-, -SO$_2$-, -NR$^{4-11-1}$-, carbonyl, -NR$^{4-11-1}$SO$_2$-, carbonylamino or aminocarbonyl, $R^{4-11-1}$ is hydrogen atom, C1-10 alkyl or C2-10 acyl, $W^{4-2}$ is C1-8 alkyl optionally substituted by C1-4 alkyl, halogen or hydroxy, $E^{4-2}$ is $U^{4-1}$-$U^{4-2}$-$U^{4-3}$ or ring 4, $U^{4-1}$ is C1-4 alkylene, C2-4 alkenylene, C2-4 alkynylene, -ring 3-, C1-4~~

~~alkylene-ring 3-, C2-4 alkenylene-ring 3- or C2-4 alkynylene-ring 3-, $U^{4-2}$ is a bond, -$CH_2$-, -CHOH-, -O-, -S-, -SO-, -$SO_2$-, -$NR^{4-12}$-, carbonyl, -$NR^{4-12}SO_2$-, carbonylamino or aminocarbonyl, $R^{4-12}$ is hydrogen atom, C1-10 alkyl or C2-10 acyl, $U^{4-3}$ is C1-8 alkyl optionally substituted by 1 to 3 substituents selected from C1-10 alkyl, halogen, hydroxy, alkoxy, alkylthio and -$NR^{4-13}R^{4-14}$, C1-8 alkenyl optionally substituted by 1 to 3 substituents selected from C1-10 alkyl, halogen, hydroxy, alkoxy, alkylthio and -$NR^{4-13}R^{4-14}$, C1-8 alkynyl optionally substituted by 1 to 3 substituents selected from C1-10 alkyl, halogen, hydroxy, alkoxy, alkylthio and -$NR^{4-13}R^{4-14}$, C1-8 alkyl substituted by ring 4 or ring 4, $R^{4-13}$ and $R^{4-14}$ are, each independently, halogen atom or C1-10 alkyl, ring 1, ring 2, ring 3 and ring 4 may be substituted by 1 to 5 substituents selected from C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C1-10 alkoxy, C1-10 alkylthio, halogen atom, hydroxy, nitro, -$NR^{4-15}R^{4-16}$, C1-10 alkyl substituted by C1-10 alkoxy, C1-10 alkyl substituted by 1 to 3 halogen atoms, C1-10 alkyl substituted by C1-10 alkoxy substituted by 1 to 3 halogen atoms, C1-10 alkyl substituted by -$NR^{4-15}R^{4-16}$, ring 5, -O-ring 5, C1-10 alkyl substituted by ring 5, C2-10 alkenyl substituted by ring 5, C2-10 alkynyl substituted by ring 5, C1-10 alkoxy substituted by ring 5, C1-10 alkyl substituted by -O-ring 5, $COOR^{4-17}$, C1-10 alkoxy substituted by 1 to 4 halogen atoms, formyl, C1-10 alkyl substituted by hydroxy or C2-10 acyl, $R^{15}$, $R^{16}$ and $R^{17}$ are, each independently, (1) hydrogen atom or (2) C1-10 alkyl, $R^{4-15}$, $R^{4-16}$ and $R^{4-18}$ are, each independently, hydrogen atom or C1-10 alkyl, ring 5 may be substituted by 1 to 3 substituents selected from C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C1-10 alkoxy, C1-10 alkyl substituted by C1-10 alkoxy, halogen atom, hydroxy, C1-10 alkyl substituted by 1 to 3 halogen atom and C1-10 alkyl substituted by C1-10 alkoxy substituted by 1 to 3 halogen atoms, ring 1, ring 2, ring 3, ring 4 and ring 5 are, each independently, C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated or 3 to 15 membered mono-,~~

~~bi- or tri-heterocyclic aryl containing hetero atoms selected from 1 to 4 nitrogen, 1 to 2 oxygen and/or 1 to 2 sulfur atom which may be partially or fully saturated. With the proviso that, when $E^4$ is $E^{4-2}$, $E^{4-2}$ is $U^{4-1}$-$U^{4-2}$-$U^{4-3}$, and $U^{4-1}$ is C2 alkylene or C2 alkenylene, $U^{4-2}$ is not -CHOH-; when $U^{4-3}$ is C1-8 alkyl substituted by at least one hydroxy, $U^{4-1}$-$U^{4-2}$ is not C2 alkylene or C2 alkenylene; when $A^4$ is $A^{4-1}$ and $D^4$ is $D^{4-1}$, $E^4$ is not $E^{4-1}$; when $T^4$ is oxygen atom, $X^4$ is $-CH_2-$, $D^4$ is $D^{4-1}$, $D^{4-1}$ is COOH, $A^4$ is $A^{4-1}$, $A^{4-1}$ is C2-8 straight-chain alkylene, $E^4$ is $E^{4-2}$, $E^{4-2}$ is $U^{4-1}$-$U^{4-2}$-$U^{4-3}$, $U^{4-1}$ is C1-4 alkylene and $U^{4-3}$ is C1-8 alkyl, $U^{4-2}$ is not a bond, $-CH_2-$, $-NR^{12}-$ or carbonyl; when $T^4$ is oxygen atom, $X^4$ is $-CH_2-$, $D^4$ is $D^{4-1}$, $D^{4-1}$ is COOH, $A^4$ is $A^{4-2}$, $G^{4-1}$ is C1-4 alkylene, $G^{4-2}$ is -O- or $-NR^{4-1}-$, $G^{4-3}$ is a bond or C1-4 alkylene, $E^4$ is $E^{4-2}$, $E^{4-2}$ is $U^{4-1}$-$U^{4-2}$-$U^{4-3}$, $U^{4-1}$ is C1-4 alkylene and $U^{4-3}$ is C1-8 alkyl, $U^{4-2}$ is not a bond, $-CH_2-$, $-NR^{4-12}-$ or carbonyl; when $T^4$ is oxygen atom, $X^4$ is $-CH_2-$, $D^4$ is $D^{4-1}$, E is $E^{4-2}$, $E^{4-2}$ is $U^{4-1}$-$U^{4-2}$-$U^{4-3}$, $U^{4-1}$ is C2 alkylene or C2 alkenylene and $U^{4-2}$ is -CO-, $A^4$ is not $A^{4-1}$,~~

~~or a salt thereof,~~ and a pharmaceutically acceptable carrier,

to a subject in need of stimulating chondrocyte growth,

wherein said cartilage-related disease is selected from rheumatoid arthritis, osteoarthritis, cartilage damage, articular disk damage, meniscus injury, chondrodysplasia, achondroplasia, achondrogenesis, dyschondrogenesis, chondrodystrophia, articular chondrocalcinosis, acute purulent arthritis, tuberculous arthritis, syphilitic arthritis, systemic lupus erythematosus, spondylosis deformans, disk herniation, injury by sports and keypuncher's disease.

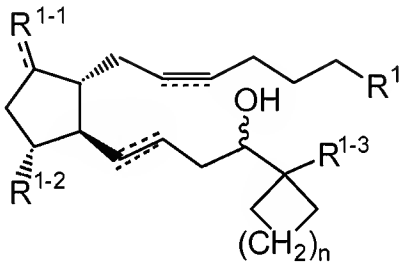
36. (Currently amended) The method according to claim 35, wherein the compound represented by formula (1-1)~~substance having an EP2 agonist activity~~ is one or more compounds selected from

(1) (5Z,9β,11α,13E)-17,17-propano-11,16-dihydroxy-9-chloro-20-norprosta-5,13-dienoic acid, and

(2) (5Z,9β,11α,13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid,

or a salt thereof.

37. (New) A method for treating cartilage disorder, which consists of administering a composition consisting of a compound represented by formula (1-1)



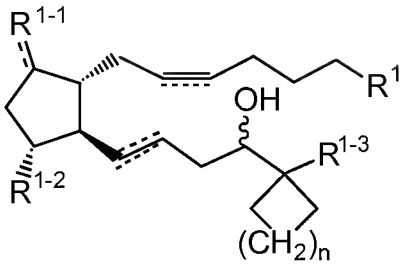

(1-1)

wherein all symbols have the same meanings as those described in Claim 35

or a salt thereof, and a pharmaceutically acceptable carrier,

to a subject in need of stimulating chondrocyte growth.

38. (New) A method for stimulating chondrogenesis, stimulating chondrocyte growth, stimulating chondrocyte differentiation, inhibiting cartilage calcification and/or inhibiting cartilage degradation, which consists of administering a composition consisting of a compound represented by formula (1-1)



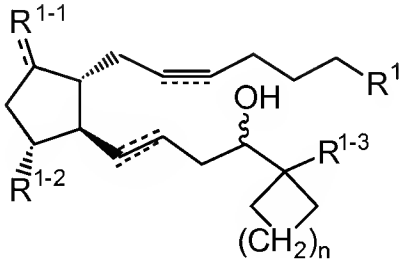

(1-1)

wherein all symbols have the same meanings as those described in Claim 35

or a salt thereof, and a pharmaceutically acceptable carrier,

to a subject in need of stimulating chondrocyte growth.

39. (New) A method for stimulating integrin mRNA expression, stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and/or inhibiting osteopontin mRNA expression, which consists of administering a composition consisting of a compound represented by formula (1-1)




(1-1)

wherein all symbols have the same meanings as those described in Claim 35

or a salt thereof, and a pharmaceutically acceptable carrier,

to a subject in need of stimulating chondrocyte growth.

40. (New) The method according to claim 38, wherein one or more selected from the stimulation of chondrogenesis, stimulation of chondrocyte growth, stimulation of chondrocyte differentiation, inhibition of cartilage calcification, and inhibition of cartilage degradation is/are

correlated with one or more selected from actions of stimulating integrin mRNA expression, stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression on a chondrocyte or a cartilage tissue, by the composition of claim 38.

41. (New) The method according to claim 40, wherein the stimulation of chondrocyte growth is correlated with the action of stimulating cyclin D1 mRNA expression by the composition of claim 38.

42. (New) The method according to claim 40, wherein the inhibition of cartilage calcification is correlated with the action of inhibiting osteopontin mRNA expression by the composition of claim 38.